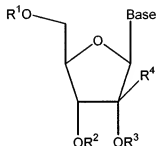


### AMENDMENTS TO THE CLAIMS

1-32. (Canceled)

33. (Currently Amended) A method for treating a hepatitis C virus infection in a host, comprising (a) administering an effective amount of a 2'-branched nucleoside of the formula:



or a pharmaceutically acceptable prodrug or salt thereof to the host, wherein

R<sup>1</sup> and R<sup>2</sup> are independently H; mono, di or triphosphate; acyl; sulfonate ester; benzyl; an amino acid ester; a carbohydrate; a peptide; a cholesterol or a pharmaceutically acceptable leaving group that provides a compound wherein R<sup>1</sup> or R<sup>2</sup> is independently H or phosphate when administered *in vivo*;

R<sup>3</sup> is hydrogen;

R<sup>4</sup> is alkyl, alkenyl, or alkynyl; and

Base is a pyrimidine;

- (b) identifying viral resistance to the 2'-branched nucleoside in the host by detecting an amino acid 282 Ser to Thr mutation in the RNA polymerase region of the hepatitis C virus; and

- (c) administering to the host infected with the virus resistant to the 2'-branched nucleoside, an effective amount of one or more drugs that directly or indirectly induce a mutation in a hepatitis C virus at a location other than nucleotide 8443 (G to C) of the HCV genome or amino acid 282 Ser to Thr of the RNA polymerase region of HCV.

34.-37. (Canceled).

38. (Previously Presented) The method of claim 33, wherein the 2'-branched nucleoside is  $\beta$ -D-2'-CH<sub>3</sub>-riboC, or a phosphate thereof, or a pharmaceutically acceptable salt or ester thereof.
39. (Previously Presented) The method of claim 33, wherein the 2'-branched nucleoside is a 3'-amino acid prodrug of  $\beta$ -D-2'-CH<sub>3</sub>-riboC.
40. (Previously Presented) The method of claim 39, wherein the 2'-branched nucleoside is a 3'-L-valinyl prodrug of  $\beta$ -D-2'-CH<sub>3</sub>-riboC.
41. – 86. (Canceled).
87. (Previously Presented) The method of claim 33, wherein R<sup>1</sup> is a mono, di or triphosphate.
88. (Canceled).
89. (Previously Presented) The method of claim 33, wherein R<sup>2</sup> is an amino acid ester.
90. (Canceled).
91. (Canceled).
92. (Previously Presented) The method of claim 33, wherein R<sup>4</sup> is methyl.
93. – 100. (Canceled).
101. (Previously Presented) The method of claim 33, wherein R<sup>2</sup> is an ester of a naturally occurring or synthetic  $\alpha$ ,  $\beta$ ,  $\gamma$ , or  $\delta$  amino acid.
102. (Canceled).
103. (Previously Presented) The method of claim 33, wherein R<sup>2</sup> is an ester of valine.

104. (Previously Presented) The method of claim 33, wherein  
R<sup>4</sup> is methyl;  
R<sup>2</sup> is acyl or an amino acid ester;  
R<sup>3</sup> is H; and  
R<sup>1</sup> is H.
105. (Previously Presented) The method of claim 104, wherein R<sup>2</sup> is an amino acid ester.
106. (Previously Presented) The method of claim 104, wherein R<sup>2</sup> is an ester of valine.
107. (Previously Presented) The method of claim 33 wherein the host is human.
108. (Canceled).
109. (Previously Presented) The method of claim 33, wherein the 2'-branched nucleoside is in a pharmaceutically acceptable carrier or diluent.
110. (Previously Presented) The method of claim 33, wherein the drug in step (c) is interferon.
111. (Previously Presented) The method of claim 33, wherein identifying viral resistance in step (b) comprises assaying the blood of the host to test for seroconversion from wildtype to mutant hepatitis C virus.
112. (Previously Presented) The method of claim 33, wherein identifying viral resistance in step (b) comprises phenotypic analysis of viral plaque growth from a viral culture sample from the host.
113. (Previously Presented) The method of claim 112, wherein the phenotypic analysis of step (b) comprises  
(i) obtaining a viral culture sample from the host;

- (ii) culturing the sample and comparing the plaque growth between the sample and wild type virus; and
- (iii) determining whether the plaque growth of the sample is smaller than the plaque growth of the wildtype virus.

114. (Previously Presented) The method of claim 33, wherein identifying viral resistance in step (b) comprises determination of the replication fitness of the virus.

115. (Previously Presented) The method of claim 114, wherein determination of the replication fitness of the virus in step (b) comprises

- (i) obtaining a viral culture sample from the host;
- (ii) determining the replication fitness of the sample virus; and
- (iii) determining whether the replication fitness of the sample virus is less than the replication fitness of the wildtype virus.

116. (Previously Presented) The method of claim 33, wherein identifying viral resistance in step (b) comprises detecting the presence of cytidine at nucleotide 8443 of the RNA polymerase region of the hepatitis C virus.

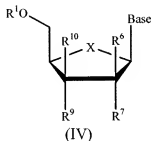
117. (Currently Amended) The method of claim 33, wherein identifying viral resistance in step (b) comprises

- (i) contacting a sample containing a hepatitis C virus nucleic acid sequence with a detectable oligonucleotide probe having a sequence complementary to a codon that encodes a serine in the highly conserved consensus sequence, XRXSGXXX<sup>T</sup>, of domain B of the RNA polymerase region of the hepatitis C virus;
- (ii) allowing the probe to hybridize to the sequence; and
- (iii) detecting the hybridization of the probe the sequence.

118. (Currently Amended) A method of treating a hepatitis C virus infection in a host infected with a hepatitis C virus that contains a mutation at nucleotide 8443 (G to C) of the HCV genome or amino acid 282 Ser to Thr of the RNA polymerase region of HCV, comprising administering to the host infected with said virus an effective amount of one or more drugs that directly or indirectly induce a mutation in a hepatitis C virus at a location other than nucleotide 8443 (G to C) of the HCV genome or amino acid 282 Ser to Thr of the RNA polymerase region of HCV.

119. (Previously Presented) The method of claim 117, wherein the drug is interferon.

120. (Currently Amended) A method for treating a hepatitis C virus infection in a host, comprising (a) administering an effective amount of a 2'-branched nucleoside of formula IV:



or a pharmaceutically acceptable prodrug or salt thereof to the host, wherein:

Base is a pyrimidine;

$R^6$  is alkyl,  $CH_3$ ,  $CF_3$ , azido, cyano, alkenyl, alkynyl, Br-vinyl, 2-Br-ethyl,  $-C(O)O(alkyl)$ ,  $-C(O)O(lower\ alkyl)$ ,  $-O(acyl)$ ,  $-O(lower\ acyl)$ ,  $-O(alkyl)$ ,  $-O(lower\ alkyl)$ ,  $-O(alkenyl)$ ,  $CF_3$ , fluoro, chloro, bromo, iodo,  $NO_2$ ,  $NH_2$ ,  $-NH(lower\ alkyl)$ ,  $-NH(acyl)$ ,  $-N(lower\ alkyl)_2$ ,  $-N(acyl)_2$ ;

$R^7$  is  $OR^2$ , hydroxy, alkyl, azido, cyano, alkenyl, alkynyl, Br-vinyl, halo-vinyl,  $-C(O)O(alkyl)$ ,  $-C(O)O(lower\ alkyl)$ ,  $-O(acyl)$ ,  $-O(lower\ acyl)$ ,  $-O(alkyl)$ ,  $-O(lower\ alkyl)$ ,  $-O(alkenyl)$ , fluorine, chlorine, bromine, iodine,  $NO_2$ ,  $NH_2$ ,  $-NH(lower\ alkyl)$ ,  $-NH(acyl)$ ,  $-N(lower\ alkyl)_2$ ,  $-N(acyl)_2$ ;

$R^9$  is hydrogen,  $OR^3$ , hydroxy, alkyl, azido, cyano, alkenyl, alkynyl, Br-vinyl,  $-C(O)O(alkyl)$ ,  $-C(O)O(lower\ alkyl)$ ,  $-O(acyl)$ ,  $-O(lower\ acyl)$ ,  $-O(alkyl)$ ,  $-O(lower\ alkyl)$ ,  $-O(alkenyl)$ ,

chlorine, bromine, iodine, NO<sub>2</sub>, NH<sub>2</sub>, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)<sub>2</sub>, -N(acyl)<sub>2</sub>;

R<sup>10</sup> is H, alkyl, fluorine, chlorine, bromine or iodine;

R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are independently H, phosphate; straight chained, branched or cyclic alkyl; acyl; CO-alkyl, CO-aryl, CO-alkoxyalkyl, CO-aryloxyalkyl, CO-substituted aryl, sulfonate ester; benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; alkylsulfonyl, arylsulfonyl, aralkylsulfonyl, lipid; amino acid; carbohydrate; peptide; cholesterol; or a pharmaceutically acceptable leaving group that provides a compound wherein R<sup>1</sup>, R<sup>2</sup> or R<sup>3</sup> is independently H or phosphate when administered *in vivo*; and

X is O, S, SO<sub>2</sub> or CH<sub>2</sub>;

(b) identifying viral resistance to the 2'-branched nucleoside in the host by detecting an amino acid 282 Ser to Thr mutation in the RNA polymerase region of the hepatitis C virus; and

(c) administering to the host infected with the virus resistant to the 2'-branched nucleoside, an effective amount of one or more drugs that directly or indirectly induce a mutation in a hepatitis C virus at a location other than nucleotide 8443 (G to C) of the HCV genome or amino acid 282 Ser to Thr of the RNA polymerase region of HCV.

121. (Previously Presented) The method of claim 33, wherein the compound according to the formula is administered.

122. (Previously Presented) The method of claim 120, wherein the compound according to Formula IV is administered.